## REMARKS

Claims 23-32 are pending.

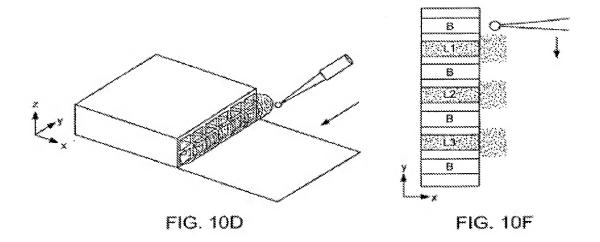
Previous claims 1, 2, 15, 16, 21 and 22 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. (20040181343). Claims 5 and 17-19 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. in view of Knapp et al (U.S. 6,444,461). Claims 6-9, 11-14 and 20 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. in view of Graves (U.S. 4,829,009). Claim 10 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Wigstrom et al. in view of Graves and further in view of Knapp et al.

Each of the foregoing rejections <u>continues</u> to be premised on a fundamental misapprehension, if not disregard, of the plain and contrary teaching of Wigstrom, as was described with some detail in Applicant's remarks submitted September 24, 2009, which remarks are virtually ignored in the December 30, 2009 Official action. Each of the standing rejections plainly lacks merit and should be withdrawn.

As Applicant has consistently shown, and the Examiner consistently disregarded, Wigstrom fails to disclose either a mechanism or step for temporarily reducing the amount of liquid in a detection area in the course of the detection. The Official action acknowledges that deficiency and, remarkably and incorrectly, contends that the method claims "do not require detection of material where the liquid is reduced." (Dec. 30)

Official action, p. 10). To the contrary, all of the claims, including those previously presented as well as those now pending, recite that the detection takes place at a defined portion of the substrate on which the fluid has been temporarily reduced. Wigstrom lacks any teaching or suggestion of that aspect of the claimed invention, and any modification to Wigstrom to provide that capability (which in any event the Official action fails to attempt to identify) would be directly contrary to the express intentions stated in that reference.

Wigstrom discloses a microfluidic substrate having a plurality of parallel fluid microchannels opening to a chamber. Each microchannel delivers to the chamber a steady state fluid stream of either a test liquid or a buffer. A "sensor" in the form of one or more molecules is carried by a micropositioner. The microfluidic substrate and the micropositioner are movable relative to each other such that the sensor molecule can be scanned across each emerging fluid stream. These features of Wigstrom's device are plainly shown in Figures 10D and 10F of that reference, which are reproduced below:



To provide for the necessary movement of the sensor across the emerging streams, Wigstrom teaches that the microfluidic substrate may be moved in an x-, y-, and/or z- direction and may also be tilted. See Wigstrom at paragraph 89.

In contrast, the instant claims recite a mechanism adapted for (or step of) temporarily reducing the amount of liquid containing the second species in a detection zone during the detection. As the application plainly explains, this temporary reduction is beneficial for reducing the signal otherwise generated by the unbound ligand contained in the liquid, without requiring the complete removal of liquid or intermediate washing of the target species with a different liquid. See, e.g., page 5, lines 1-5, page 9, lines 13-24 and page 12, line 3 to page 13, line 27. Neither Wigstrom nor any of the secondary references relied upon by the Official Action mentions or enables this temporary reduction of fluid during a detection.

To attempt to cure that deficiency, the Official Action relies on Wigstrom's disclosure of "tilting" for the purpose of scanning a sensor across the plurality of fluid streams. However, any mechanism for tilting as disclosed by Wigstrom would necessarily preserve the steady flow of the emerging fluid streams. Accordingly, the tilting feature in Wigstrom plainly is not adapted for temporarily reducing fluid, much less reducing that fluid in the course of a detection.

Wigstrom requires that each fluid stream emerges "at the same rate" so as to establish "steady state concentrations." (Paragraph 104). Thus, tilting Wigstrom's substrate would not temporarily reduce the amount of liquid in the detection area and Wigstrom explicitly teaches against that result. The Official Action fails to address this contrary requirement of Wigstrom.

The Official Action alternatively contends, relying on Graves, that it would have been obvious to "utilize the Wigstrom et al. device to make detections as suggested by Graves in order to detect background noise that may interfere with the assay results." (Dec. 30 Official Action, page 12.) However, Graves fails to teach or suggest temporarily reducing liquid present during the course of a detection. Accordingly, the combination of the disclosure of Graves with Wigstrom, which likewise fails to teach or suggest temporarily reducing liquid present during the course of a detection, fails to render the instant claims unpatentable.

The measurement principle of Wigstrom is based on repeatedly substituted different liquids, such that equilibrium conditions for the detected complex would be repeatedly disrupted. The present invention, in contrast, is performed repeatedly in the same liquid, over a period of time and in a temporarily reduced amount, thereby preserving the equilibrium conditions for the complex.

As noted in the remarks submitted September 24, 2009, Neither Wigstrom's intermediate wash streams nor the contrivance of the Official Action involving removing fluid from the channels even remotely satisfies the present recitations which enable a reference area and target area to be detected under the same fluid, not to mention that the amount of fluid is temporarily reduced during the detection.

Wigstrom, either alone or in combination with any of the cited secondary references, plainly lacks that presently recited feature that liquid at a detected portion of the substrate is temporarily reduced during the detection. The cited reference further lacks numerous other features that are recited in the claims of this application which are not even addressed in the Official Action.

For example, instant claim 1 recites a solid support "on which said first species can be attached in one or more non-overlapping defined areas thereon" and in which "at least one of the defined areas does not have said first species attached."

These recitations are neither shown nor suggested by the very different structure (and purpose) of Wigstrom.

Wigstrom discloses a support (the microfluidic substrate) that is not adapted to have any target species attached. Indeed, it is essential in Wigstrom that the species is not attached to the microfluidic substrate so that it may be scanned across the emerging fluid streams. The previous Official Action conceded this point at page 3 where it was acknowledged that "Wigstrom et al. further disclose a 'sensor chamber' which receives sensors."

Thus, Wigstrom fails to disclose a support on which a first species can be attached at one defined area and not attached at a different, reference area. None of the rejections set forth in the Official action even attempt to address this fundamental distinction of Wigstrom from the present claims.

In view of the foregoing remarks, it is believed that the present application is in condition for allowance. Reconsideration and allowance are respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

Docket No. 1510-1120 Appln No. 10/588,011

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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